concentrations in these regions of the intestines when these microparticles are used as carriers of immunogens for oral or other types of immunization.

If the microspheres do not have the correct average particle size distribution, the inventors found that they will not be taken up by the M cells and non-M cells, either in the villous epithelium or in the Peyer's patches follicle associated epithelium. If this does not occur, the uptake of the antigens or other chemotherapeutic agents within these microspheres is inefficient and large doses of same are required to have any effect.

The size of microspheres at issue in the claims is 0.5 to 2.0 micrometers for the villous epithelium section of the intestines of a mammal and 1.0 to 7.0 micrometers for the Peyer's patch section of an intestine of a mammal. These are very small sizes and consequently are difficult to make. Applicants have accomplished the production of these small sizes by the method disclosed in the instant specification in the detailed description, column 4, line 45 through column 6, line 35.

No where in Tice, et al. is there any teaching or suggestion to produce an average particle size distribution of 0.5 to 2.0 micrometers or 1.0 to 7.0 micrometers or any discussion to chooses an average particle size distribution to be taken up by the Peyer's patch or villous epithelium section of the intestine. On the contrary, Tice, et al. discusses using a syringe rather than an oral dose. Tice et al. is only concerned with particles small enough to go through a syringe, not small enough to be taken up by the M cells and non M cells of the intestines. Therefore, Tice et al. would not have motivated one of ordinary skill in the art to produce the average particle size distribution claimed by Applicants.

Further, the method of producing microspheres in Tice, et al. uses a sieving procedure (column 7, lines 1-5) that is not required in the instant invention. It is questionable whether a sieving procedure will even result in submicron particles. There is also no teaching in Tice et al. that a sieving process will produce the claimed submicron average particle size distribution.

In summary, the language of claims 17-24, "average particle size distribution wherein a majority of the microspheres will be taken up by a villous epithelium section of the intestines" (claims 17 and 19) or "average particle size distribution wherein a majority of the microspheres will be taken up by a Peyer's patch section of an intestine" (claim 18 and 22) and the average particle distribution size ranges in claims 21 and 24 is

not disclosed or suggested by Tice et al. For Tice, et al. to be a proper reference, there must be some teaching in Tice et al. to lead one of ordinary skill in the art to the claim language of the present invention. There is simply no teaching of targeting the M cells and non M cells with a particular size range of microspheres to be taken up by the claimed sections of the intestines. Hence, the rejection under 35 U.S.C. §103(a) should respectfully be removed.

Respectfully submitted,

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